

Epidemiological, clinical, and toxicological studies have demonstrated

adverse pulmonary and cardiovascular health effects associated with

ambient air PM exposure. Many of these studies have identified ambient air PM size, metal content\bioavailability, or endotoxin content

as causal particulate properties. However, ambient air PM represents

an highly dynamic and physicochemically complex mixture containing

additional causal properties which have yet to be identified. PM

toxicological studies provide an approach to: 1) discover additional PM

causal properties; 2) assess the potential effects which copollutants/atmospheric processes have on modulating the toxicity of

established causal ambient air PM properties; and 3) assess the health

effects and hazard identification of particles derived from the combustion of contemporary and alternative fuels as well as the impact

of combustion conditions and air pollution control devices/strategies

on particle physicochemistry and toxicity. Information derived from

these studies will link adverse ambient air PM health effects to sources

as well as provide a health effects approach to evaluate\characterize

1. PM Hazard Identification - evaluate the role of organics in ambient

2. Identify PM Co-Pollutant Effects - assess the ability of co-pollutants

3. Comparative Combustion PM Toxicology - examine the effect which

combustion conditions and alternative fuel sources have on the acute

Experimental Approaches

PM Sources: Bulk and size-fractionated ambient air PM samples were

obtained from NIST, Washington DC and Ottawa, Canada, Primary fine

(PM<2.5) residual oil and Orimulsion® particles were obtained from the

US EPA, National Risk Management Research Laboratory (NRMRL), Air

Pollution Prevention Control Division (APPCD). PM samples were

analyzed for: acid and water soluble metals content, elemental and

In Vivo Toxicological Studies: Healthy rats (SD, male, 60 dy old) were

exposed to various ambient air PMs, oil combustion particles, or

surrogate metal mixtures by intratracheal instillation. Saline instilled

animals served as the control group. Control and exposed animals

were examined by bronchoalveolar lavage (BAL) at 24h post-exposure.

BAL fluid (BALF) samples were examined for biomarkers of injury such

as alterations in protein and cellular content using routine clinical

to regulate causal ambient air PM constituents such as metals:

pulmonary toxicity of oil combustion particulate emissions.

PM emission control strategies.

air PM-induced lung injury;

Toxicological studies were conducted for:

organic carbon content, and size distribution.

PARTICULATE MATTER

Emission and Ambient Air Particulate Matter Hazard Identification: Linking Adverse Health Effects to Sources

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AMBIENT AIR PM HAZARD IDENTIFICATION

Organic compounds make up a significant portion of ambient air PM mass. Organic constituents have been shown to play a significant role in the cancer and immune modulatory effects of diesel exhausts particles. However, the role organics play in ambient air PM-induced pulmonary toxicity has not been extensively studied. Identification of causal ambient air PM-associated organic constituents could provide a link to specific sources.

Volatile Organic Constituents and PM-Induced Lung Injury

Table 1 Effect of Heat on Ambient Air PM Lung Injury and Carbon Chemistry

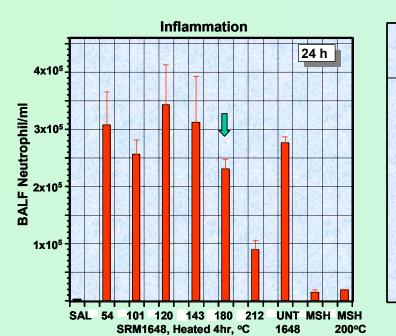
Ambient Air PM	% Decrease in PM Weight	% Decrease in BALF PMN/ml	Before ¹ Heating PM:		After Heating PM:	
Sample/Size	After Heating	After Heating	EC	oc	EC	oc
MSH	1.6	0	0	0	0	0
NIST SRM1648 (TSP)	9.8	65	6	6	8	4
NIST SRM1648(PM _{0.4-3.3})	9.4	45	12	8	14	4
NIST SRM1649(PM _{0.4-3.3})	9.4	29	15	9	17	10
RTP(PM _{<1.7})	14	62	13	14	15	9
Ottawa(PM _{0.4-3.3})	11.5	0	3	6	3	5

1. PM samples were heated at 200 – 205°C for 4h. Alterations in the acute pulmonary toxicity, PM weight, % elemental (EC), and organic (OC) carbon content were examined for heated and unheated PM samples. In 3 out of 4 ambient PM samples heat treatment produced a decrease in the amount of pulmonary nuetrophilic influx as well as a decrease in OC and an increase in EC. These toxicological "discovery based" findings suggest a possible role for PM-associated volatile organics (VOCs) in PM-induced acute pulmonary inflammation.

Table 2. Effect of Heat on Ambient Air PM Physicochemical Pror

Effect of Heat on Ambient Air PM Physicochemical Properties ¹											
PM	Water	Soluble	PM Size								
Sample	Fe	Cu	Zn	Sulfate	MMAD	GSD					
MSH	1.38	0.006	0.012	0.43	2.487	1.478					
MSH+heat	1.33	0.004	0.015	0.35	2.761	1.666					
SRM1648TSP	7.0	0.37	3.6	6.3	2.645	1.764					
SRM1648TSP+heat	10.8	0.37	3.9	6.7	2.990	1.772					
SRM1648(PM _{0.4-3.3})	10.7	0.96	4.8	238	2.106	1.571					
SRM1648(PM _{0.4-3.3})+heat	10.9	0.87	5.1	244	2.097	1.569					
SRM1649(PM _{0.4-3.3})	9.2	0.27	0.87	119	2.559	1.610					
SRM1649(PM _{0.4-3.3})+heat	10	0.24	0.95	117	2.299	1.585					
RTP(PM _{<1.7})	5.9	0.71	1.7	190	3.406	1.742					
RTP(PM _{<1.7})+heat	6.2	1.00	1.9	203	2.469	1.655					
Ottawa(PM _{0.4-3.3})	7.5	0.97	10.3	216	2.932	1.650					

1. The water soluble metal content and size of heated and unheated PM samples were determined. In all cases heat treatment did not significantly alter PM water soluble metal content and had minor effect on PM size distribution.



THERMAL DESORPTION ANALYSIS OF SRM1648

RELATIVE CONCENTRATIONS (NG/NA)

Figure 1. Identification of Causal PM Constituents. PM heat treatment was found to have a greater effect on PM organic carbon content (Table 1 and Table 2) suggesting that volatile organic compounds may mediate a significant part of the acute pulmonary inflammatory response induced by ambient air PM. NIST SRM1648 (TSP sample collected from St. Louis, MO) and Mt. St. Helen's (MSH, negative control) were heated at various temperatures and the effects on pulmonary toxicity and organic constituents were evaluated. Heating had no effect on MSH pulmonary toxicity. However, as previously reported, heating SRM1648 at 212°C was found to significantly inhibit the ability of this PM to induce an acute inflammatory response when compared to unheated SRM`1648 (UNT 1648). Thermal desorption analysis of PM samples heated at various temperatures has identified several potential causal organic constituents of SRM1648.

NOTE: Arrow indicates the temperature, 180°C, at which dry LPS (endotoxin) is functionally inactivated, at this temperature no effect on the ability of SRM1648 to induce a pulmonary inflammatory response was observed suggesting that endotoxin is not a causal component of SRM1648 for this response.

CO-POLLUTANTS MODULATE CAUSAL PM CONSTITUENTS

PM constituents are derived from a variety of primary emission sources and secondary atmospheric transformation processes of gaseous air pollutants such as sulfur dioxide, ammonia, and nitrogen dioxide. Controlled toxicological studies were conducted in order to determine the potential role secondary atmospheric transformation processes play in regulating PM causal constituents such as metals.

Acidity Enhances Metal Bioavailability and Acute Pulmonary Toxicity

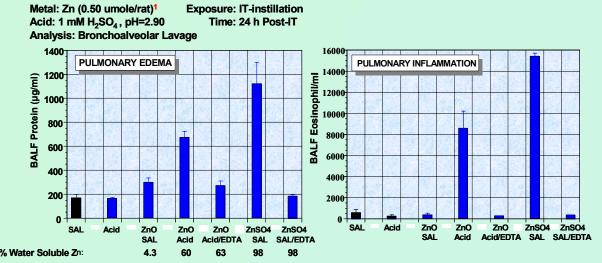


Figure 2. Acidity Enhances Metal Bioavailability and Pulmonary Toxicity.

Rats were exposed to an equivalent amount of Zn in the form of ZnO in the presence and absence of sulfuric acid, a atmospheric transformation by-product of SO2, with or without EDTA. Acid enhanced the bioavailability of Zn as well as its acute pulmonary toxicity suggesting that combustion processes that generate SO2 or NO2 in combination with secondary acidic transformation processes have the potential of enhancing the bioavailability and pulmonary toxicity of ambient air PM-associated metals.

2º PM-Associated Constituents Modulate Metal Pulmonary Toxicity

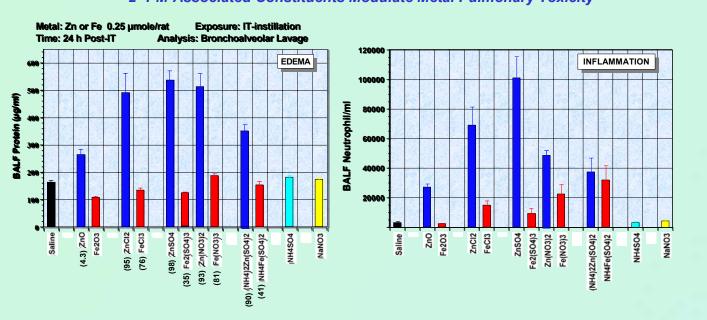


Figure 4. Effect of chemical composition and bioavailability on Zn and Fe acute lung injury.

Metals co-exist ambient air PM with nitrate, sulfate, and ammonium that are formed by 2° aerosol or atmospheric processes which may regulate PM-associated metal toxicity. The acute lung injury induced by equivalent amounts of Fe and Zn in the presence of nitrate, sulfate, and ammonium was examined in order to assess whether these constituents altered Fe or Zn pulmonary toxicity. The more bioavailable forms of Zn and Fe (e.g., sulfates and nitrates) were found to induce a greater degree of acute lung injury than the less bioavailable forms (e.g., oxides). NH4 appeared to decrease Zn and enhance Fe acute lung injury. In addition, Zn(NO3)2 was found to produce half the amount of acute lung inflammation when compared to ZnSO4. This effect was not due to differences in bioavailability since Zn(NO3)2 and ZnSO4 had the same Zn solubility, suggesting that nitrate may attenuate Zn lung toxicity. These results suggest that 2° PM constituents derived from SO2, NO2 and NH4 emission sources can regulate PM-associated metal lung injury. Values in parenthesis indicate %Soluble Zn or Fe.

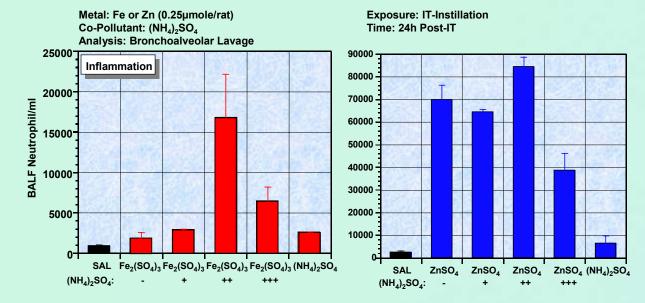
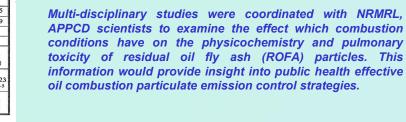


Figure 4. Effect of NH4 and/or SO4 on Zn and Fe acute lung injury.

The acute lung injury induced by equivalent amounts of Fe and Zn in the presence of increasing amounts of NH4SO4 was examined. Increasing the amount of NH4 and SO4 was found to enhance Fe and inhibit Zn acute pulmonary



COMBUSTION PM TOXICOLOGY

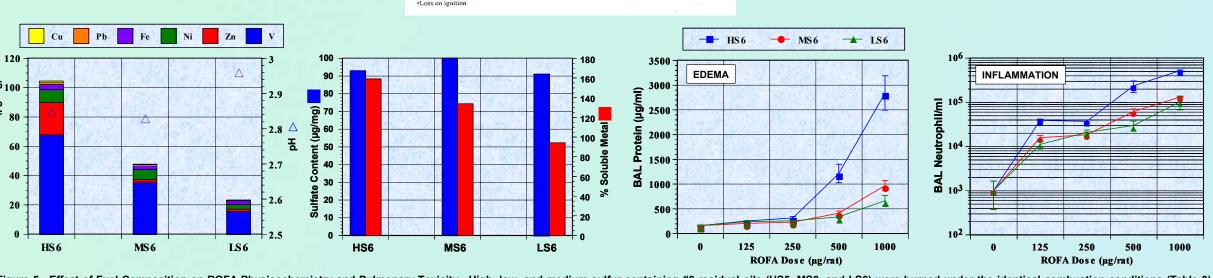


Figure 5. Effect of Fuel Composition on ROFA Physicochemistry and Pulmonary Toxicity. High, low, and medium sulfur containing #6 residual oils (HS5, MS6, and LS6) were burned under the identical combustion conditions (Table 3). PM<2.5 size fractions were collected for chemical and health effects analyses. Total and water soluble (bioavailable) metal content as well as acute pulmonary toxicity were found to correlate with residual oil sulfur content.

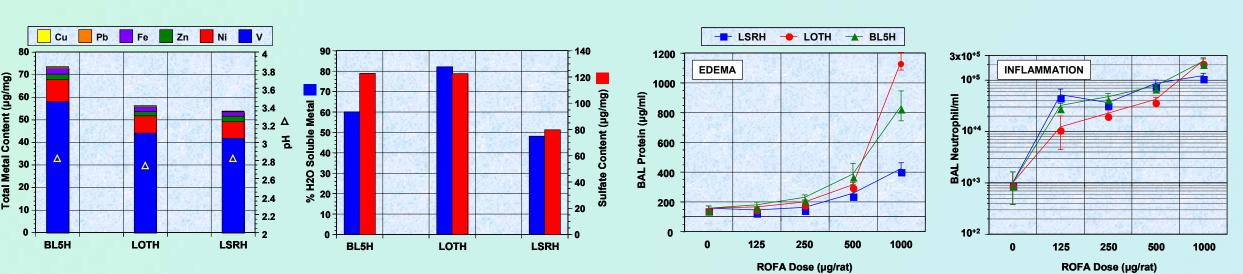


Figure 6. Effect of Combustion Conditions on ROFA Physicochemistry and Pulmonary Toxicity. The same #5 residual oil was burned under different combustion conditions (BL5H, LOTH, and LSRH, Table 3). PM<2.5 size fractions were collected for chemical and health effects analyses. Total and water soluble (bioavailable) metal content as well as acute pulmonary toxicity were significantly not different among the various #5 ROFA samples. Results obtained in Figures 5 and 6 suggest that fuel composition rather than combustion conditions have more of an impact on ROFA metal content, bioavailability and acute pulmonary toxicity.

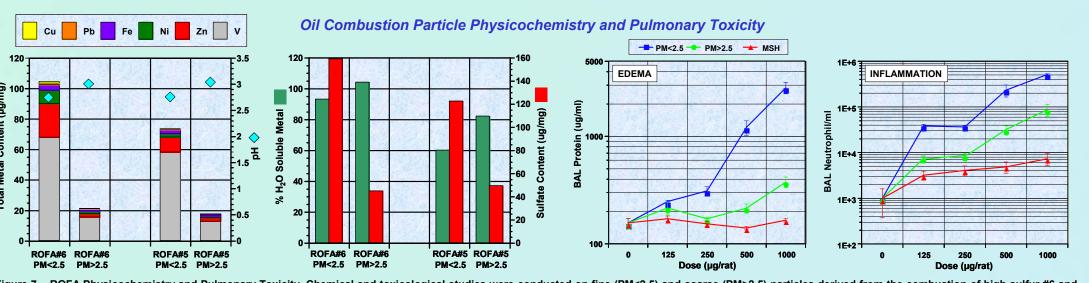


Figure 7. ROFA Physicochemistry and Pulmonary Toxicity. Chemical and toxicological studies were conducted on fine (PM<2.5) and coarse (PM>2.5) particles derived from the combustion of high sulfur #6 and #5 residual fuel oils. Elemental and toxicological studies demonstrated that fine #6 and #5 ROFAs contained higher levels of acid and water soluble (bioavailable) metals and produce correspondingly greater pulmonary toxicity when compared to coarse ROFA particles. These results suggest that pollution control strategies need to remove as much of the fine particles as possible from oil combustion emissions.

Orimulsion® Alternative Fuel Environmental Impact Assessment

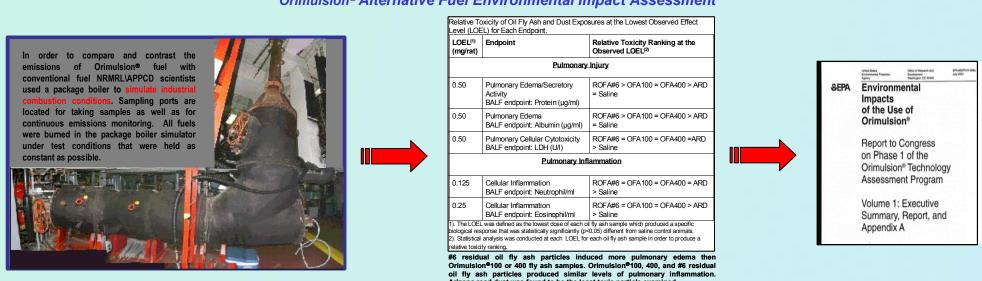


Figure 8. Pulmonary Toxicity of Alternative Fuel Sources. A coordinated multi-disciplinary study between NRMRL, APPCD, and NHEERL, ETD, PTB, scientists was undertaken to compare the emission characteristics and health effects of particles derived from the alternative fuel source Orimulsion® and conventional fuel oil. When compared to conventional fuel oil the combustion of Orimulsion® produced: 1) similar NOx, CO, and SO2 emissions; 2) higher levels of air toxics; 3) higher levels of ultrafine and fine particles with a higher metal content; and particles that were as toxic as conventional fuel oil emissions. These studies culminated in a congressional report.

CONCLUSIONS

- ► PM Hazard Identification volatile organic constituents participate in ambient air PM-induced acute pulmonary cellular inflammatory response;
- ► Co-Pollutants derived from 2° transformation processes of SO2, NO2 and NH4 modulate the acute pulmonary toxicity of metals commonly present on ambient air PM which have been found to be causal constituents in many adverse health effects;
- ► Fuel composition is more significant than combustion conditions in regulating the pulmonary toxicity of oil combustion particles;
- ▶ Fine $(PM_{<2.5})$ residual oil combustion particles are chemically distinct and display more pulmonary toxicity when compared to coarse $(PM_{>2.5})$ residual oil combustion particles.

<u>MPACT</u>

Research employing controlled PM toxicological assessment studies of ambient air PM and combustion particles have provide information which addresses NSF, NRC Research Topics #5 – Assessment of Hazardous PM Components, #7 – Effects of Co-Pollutants, and Implementation-Related Activity: Emissions, Characteristics, Factors, and Controls. In addition, a multi-disciplinary approach to assess the health impact of alternative fuel sources as well as pollution control strategies has been established.

FUTURE DIRECTIONS

Ultimately, ambient air PM-associated adverse health effects and biological responses must be linked to specific sources in order to credibly and effectively regulate particulate emission sources as well as implement effective monitoring and control strategies. Future research will focus on examining the effects which specific combustion particles have on the initiation, progression, and exacerbation of heart disease using rodent models of cardiovascular disease. Pattern recognition based bioinformatics mining of array based functional gene expression and proteomics data will be used to identify bio-response signatures indicative enhanced disease progression and susceptibility associated with specific combustion particle exposures. This research will provide a database that will allow extrapolations to be made between sources and ambient air PM induced\associated adverse cardiovascular effects and susceptibility.

